Detailed Description Text (345):
Applicants have begun to determine the spectrum of gene expression changes associated with growth suppression, morphologic alterations, increased melanin synthesis, enhanced tyrosinase activity and/or induction of terminal differentiation in human melanoma cells (12-14). The agents applicants have chosen result in reversible growth suppression, induction of melanin synthesis, morphologic alterations, enhanced tyrosinase activity, induction of a reversible commitment to differentiation or terminal differentiation with a concomitant loss of proliferative capacity in H0-1 melanoma cells (Table 2). The genes applicants have currently analyzed include: early response genes (c-fos, c-myc, c-jun, jun-B, jun-D and gro/MGSA) (14); interferon stimulated genes (ISG-15, ISG-54, HLA Class I and HLA Class II) (13, 14); cell adhesion molecules (P-cadherin, E-cadherin, N-cadherin and N-CAM) (14); extracellular matrix genes (fibronectin (FIB) and tenascin) (12, 14); cell surface proteoglycans/matrix receptors (syndecan, .beta..sub.1 integrin (major FIB receptor subunit), .alpha..sub.5 integrin (major FIB receptor subunit)) (14); cytoskeleton genes (tropomyosin-1, .gamma.-actin and .beta.-actin) (14); and a housekeeping gene (GAPDH) (14). Using the gene probes indicated above, no unique gene expression change was found which only occurred in terminally differentiated H0-1 cells. These results indicate that commitment to differentiation and terminal differentiation in H0-1 melanoma cells is associated with specific patterns of overlapping gene expression changes.
As will be discussed below, an interesting change in gene expression observed in both H0-1 cells committed to differentiate and induced to terminally differentiate was the induction and enhanced expression of type I interferon responsive genes and the gro/MGSA gene. These results have led to the hypothesis that specific autocrine feedback loops may contribute or are associated with the differentiation process in human melanoma cells.

3/23/1999